REMARKS

By Office Action mailed July 6, 2005, pending claim 42 stands rejected and claims 1-41 and 43-50 stand withdrawn, reconsideration of which is respectfully requested in view of the above amendments and following remarks. Claims 41-44 have been amended and claims 1-40 and 45-49 have been cancelled. Claims 41-44 are now pending.

Applicants' Response to Restriction Requirement

Further to Applicants' previous response to the Restriction Requirement mailed March 31, 2005, Applicants have (1) cancelled the non-elected claims, namely, claims 1-40, drawn to compounds, and claims 45-49, drawn to a method of expanding hematopoietic cell populations, and (2) amended claims 41 to 44 in order to remove the dependency of such claims on claim 40. Applicants note that no new matter has been added by way of these amendments.

With regard to Applicants' further election of the species of Example 190, disclosed in Table 15 on page 110 of the specification, and the species of adult respiratory distress syndrome, disclosed on page 32 of the specification, Applicants note that such elections were made for purposes of initial examination only and request that the Examiner consider the full scope of pending claims 41-44 in view of the above amendments and following remarks.

Objections to the Specification

(1) Applicants' claim to priority has been objected to for the reasons set forth on page 2 of the Office Action. By way of this Amendment, Applicants have amended the section entitled "Cross-Reference to Related Applications" to specify that U.S. Patent Application No. PCT/US99/24756 is a continuation-in-part of U.S. Patent Application No. 09/177,546.

(2) The specification is also objected to as not containing an abstract. By way of this Amendment, Applicants have resubmitted the Abstract previously submitted with Applicants' Preliminary Amendment filed July 20, 2001.

In view of the foregoing amendments, Applicants request that the objections to the specification be withdrawn.

Rejection under 35 U.S.C. §112, first paragraph

Claim 42 stands rejected under 35 U.S.C. §112, first paragraph, for lack of an enabling disclosure for the reasons set forth on pages 2-5 of the Office Action. More specifically, the Examiner is of the opinion that extrapolating from *in vitro* ICE inhibition to treatment of inflammatory diseases generally leads to "unpredictable" results and, therefore, undue experimentation would be required to practice the claimed invention. Applicants respectfully disagree.

As noted by the Examiner, the claimed compounds have activity as inhibitors of interleukin-1β converting enzyme (ICE) and related proteases, referred to as the ICE/ced-3 family of cysteine proteases. To this end, a number of representative compounds have been shown to inhibit ICE, as well as a number of other caspase proteases (*see* Preparation 3, and the accompanying data, set forth on pages 41-45 and 63-65).

Compounds that inhibit the ICE/ced-3 family of cysteine proteases are useful for a variety of purposes, including treatment of inflammatory diseases (as claimed in pending claim 42). For example, as demonstrated by Ku et al. (*Cytokine* 8(5):377-386, 1996 – copy attached), inhibitors of ICE block progression of type II collagen-induced arthritis (CIA) in mice. As stated by Ku et al. in the first paragraph of the "Discussion" section (*see* page 382):

> We have shown that two irreversible prototype inhibitors of ICE effectively block secretion of both IL-1 and IK-1 in vitro and provide the first evidence for efficacy of an ICE inhibitor in a chronic inflammatory disease model.

Further, as stated in the last paragraph of the Discussion section:

> The efficacy of VE-13,045 [*i.e.*, one of the test peptidyl compounds] in CIA suggests that such a compound may be suitable for clinical evaluation in patients with RA [Rheumatoid arthritis], osteoarthritis or other clinical indication where IL-1 contributes to the progression of inflammatory disease.

As a further example, in their review article, Thornberry et al. (*Science 281*:1312-1316, 1998 – copy attached) note (*see* third paragraph on page 1316):

> Excessive apoptosis has been blamed for several pathologies for which there are currently limited therapeutic options, including neurodegenerative diseases, ischemia-reperfusion injury, graft-versus-host disease, and autoimmune disorders. Caspases are attractive potential targets for the treatment of these

> conditions because of the requisite role of these enzymes in apoptosis and the appealing prospect of small-molecule inhibitory therapy. ... [For example, P]eptidyl caspase inhibitors are effective in animal models of stroke, myocardial ischemia-reperfusion injury, liver disease, and traumatic brain injury.

Accordingly, Applicants respectfully disagree with the Examiner's contention that undue experimentation would be required to practice the claimed invention, in view of the foregoing (*i.e.*, the teaching of the specification as originally filed, as further supported by the attached references) and request that this ground of rejection be withdrawn.

Rejections under 35 U.S.C. §112, second paragraph

Claim 42 stands rejected under 35 U.S.C. §112, second paragraph, as being (1) dependent on a non-elected claim, and (2) indefinite as to the intended diseases. As noted above, by way of this Amendment, Applicants have amended claim 42, as well as claims 41, 43 and 44, in order to remove the dependency of such claims on claim 40. As further noted above, Applicants' election of the species of adult respiratory distress syndrome (an inflammatory condition) was made for purposes of initial examination only and Applicants request that the Examiner consider the full scope of pending claim 42 in view of the above remarks in response to the Examiner's rejection under 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. §102(b)

Claim 42 stands rejected under 35 U.S.C. §102(b) as being anticipated by Dolle et al. (U.S. Patent No. 5,585,357) for the reasons set forth on page 6 of the Office Action. By way of this Amendment, and in order to expedite allowance of the present application, Applicants have amended claim 42, as well as claims 41, 43 and 44, to incorporate the limitations of previously pending claim 23. Applicants submit that no new matter has been added by way of these amendments. Furthermore, these amendments are not, and should not be construed as, an acquiescence to the Examiner's rejection and Applicants reserve the right to continue prosecution of the cancelled subject matter in one or more related applications. In view of the foregoing, Applicants submit that Dolle does not disclose every element of pending 42, or claims 41, 43 and 44, as amended. Accordingly, Applicants request that this ground of rejection be withdrawn.

In view of the above amendments and remarks, allowance of claims 41-44 is respectfully requested. A good faith effort has been made to place this application in condition for allowance. However, should any further issue require attention prior to allowance, the Examiner is requested to contact the undersigned at (206) 622-4900 to resolve the same. Furthermore, the Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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Enclosures:

Ku et al., "Interleukin-1ß Converting Enzyme Inhibition Blocks Progression of Type II Collagen-Induced Arthritis in Mice" (*Cytokine 8*(5):377-386, 1996)

Thornberry et al., "Caspases: Enemies Within" (*Science 281*:1312-1316, 1998)

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